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#### REMARKS

Claims 1, 3-5, 8, 9 and 12 are pending in the subject application. Applicant has hereinabove amended claims 1 and 3-5, and cancelled claims 13-19, without prejudice, as withdrawn from consideration. Accordingly, upon entry of this Preliminary Amendment, claims 1, 3-5, 8, 9 and 12 will still be pending and under examination.

In making these amendments, applicant neither concedes the correctness of the Examiner's rejections in the August 11, 2004 Final Office Action, nor abandons the right to pursue in a continuing application embodiments of the instant invention no longer claimed in this application. Applicant maintains that these amendments to claims 1 and 3-5 do not raise any issue of new matter, and that claims 1 and 3-5, as amended, are fully supported by the specification as originally filed.

Support for the claim amendments is found, inter alia, in the specification as follows: Claim 1: page 11, lines 3 and 4, page 15, lines 36 and 37, page 19, lines 25-36, page 20, lines 32-34, Figure 2A; and Claims 3-5: page 3, lines 26-31, page 5, lines 3-9 and 25-33, and page 20, lines 32-34.

In view of the arguments set forth below, applicant maintains that the Examiner's rejections made in the August 11, 2004 Final Office Action have been overcome, and respectfully requests that the Examiner reconsider and withdraw same.

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### **Formalities**

The Examiner states that claims 3-5 are objected to as depending from rejected claim 1, but would be allowable if rewritten in independent form.

In response to the Examiner's objection, but without conceding the correctness thereof, applicant has amended claims 3-5 into independent form. Thus, applicant maintains that the Examiner's objection to claims 3-5 is now obviated, and request that the Examiner reconsider and withdraw this ground of objection.

### Claim Rejection under 35 U.S.C. §102(b)

The Examiner rejected claim 1 under 35 U.S.C. §102(b) as allegedly anticipated by Wang et al. (In Vitro Cellular and Developmental Biology 27(1): 63-74, 1/1991; "Wang").

In response to the Examiner's rejection, applicant respectfully traverses.

According to M.P.E.P. §2131.01, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Thus, for Wang to anticipate the cell line of claim 1, it would have to teach each and every element thereof.

Wang fails to do this because it does not teach an immortalized human undifferentiated cardiomyocyte cell line derived from post-mitotic primary non-immortalized

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human cardiomyocytes obtained from adult human heart tissue.

Briefly, claim 1, as amended, provides for an immortalized human undifferentiated cardiomyocyte cell line, wherein the cell line comprises a replicable vector that expresses SV-40 large T antigen, and wherein the cell line is produced by a method comprising the step of fusing a post-mitotic primary non-immortalized human cardiomyocyte obtained from adult human heart tissue with a human fibroblast, the fibroblast (a) having been treated with ethidium bromide; (b) comprising a replicable vector expressing SV40 large T antigen which confers immortality on a cell comprising same; and (c) being free of mitochondrial DNA.

Wang teaches a human cardiac myocyte cell line ("W1") derived from fetal cardiac tissue, and is produced by cotransfecting fetal cardiac myocytes with the plasmids pSV2Neo and PRSVTAg, using the calcium phosphate procedure (see pages 63 [abstract] and 64). Nowhere does Wang teach a human cardiac myocyte cell line derived from adult human heart tissue. Accordingly, Wang et al. fails to anticipate the cell line of claim 1, and the Examiner has not established any teaching to the contrary.

In view of the above remarks, applicant maintains that claim 1 satisfies the requirements of 35 U.S.C. §102(b).

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# Supplemental Information Disclosure Statement

In accordance with the duty of disclosure under 37 C.F.R. \$1.56, applicants would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (EXHIBIT A). Copies to the disclosures listed below as items 1-13 are attached hereto as EXHIBITS 1-13.

- 1. Bottenstein, J., et al., "The Growth Of Cells In Serum-Free Hormone-Supplemented Media," Methods Enzymol., 58:94-109 (1979) (EXHIBIT 1);
- 2. Claycomb, W., et al., "HL-1 Cells: A Cardiac
   Muscle Cell Line That Contracts And Retains
   Phenotypic Characteristics Of Adult
   Cardiomyocytes," PNAS, 95:2979-2984 (1998)
   (EXHIBIT 2);
- 3. Cozzarelli, N.R., "The Mechanism Of Action Of Inhibitors Of DNA Synthesis," Annu. Rev. Biochem., 46:641-668 (1977) (EXHIBIT 3);
- 4. Hannon, G.J., "RNA Interference," <u>Nature</u>, 418:244-51 (2002) (**EXHIBIT 4**);
- 5. Juttermann, R., et al., "Toxicity Of 5-aza-2'-deoxycytidine To Mammalian Cells In Mediated Primarily By Covalent Trapping Of DNA Methyltransferase Rather Than DNA Demethylation, Proc. Natl. Acad. Sci. USA, 91:11797-801 (1994) (EXHIBIT 5);

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- 6. King, M.P., et al., "Human Cells Lacking mtDNA:
  Repopulation With Exogenous Mitochondria By
  Complementation," Science, 246:500-503 (1989)
  (EXHIBIT 6);
- 7. Libby, P., et al., "Long-Term Culture Of Contractile Mammalian Heart Cells In A Defined Serum-Free Medium That Limits Non-Muscle Cell Proliferation," J. Mol. Cell Cardiol., 16:803-811 (1984) (EXHIBIT 7);
- 8. Mohamed, S.N., et al., "A Serum-Free, Chemically-Defined Medium For Function And Growth Of Primary Neonatal Rat Heart Cell Cultures," <u>In Vitro</u>, 19:471-478 (1983) (**EXHIBIT 8**);
- 9. Morkin, E., "Control Of Cardiac Myosin Heavy Chain Gene Expression," Microsc. Res. Tech., 50:522-531 (2000) (EXHIBIT 9);
- 10. Nag, A.C., "Embryonic Chick Heart Muscle Cells,"

  Cell Culture Techniques In Heart And Vessel

  Research (ed. Piper, H.M.), New York: Springer
  Verlag, pages 4-19 (1990) (EXHIBIT 10);
- 11. Nag, A.C., et al., "Factors Controlling Embryonic
  Heart Cell Proliferation In Serum-Free Synthetic
  Media," In Vitro Cell Dev. Biol., 21:553-62
  (1985) (EXHIBIT 11);

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12. Singer, K., et al., "Removal Of Fibroblasts From Human Epithelial Cell Cultures With Use Of A Complement Fixing Monoclonal Antibody Reactive With Human Fibroblasts And Monocytes/Macrophages," J. Invest. Dermatol., 92:166-170 (1989) (EXHIBIT 12); and

13. Weiss, A., et al., "The Mammalian Myosin Heavy Chain Gene Family," Annu. Rev. Cell Dev. Biol., 12:417-39 (1996) (EXHIBIT 13).

No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement.

## Summary

Applicant maintains that the claims pending are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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